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(FILE 'CAPLUS' ENTERED AT 12:43:45 ON 10 AUG 2000)
L1 2715 SEA ABB=ON PLU=ON (HPV OR PAPILLOMAVIR? OR (PAPILLOMA OR WART)(W)VIRUS?)(5A)(16 OR 18 OR 31 OR 33 OR 45) OR HPV16 OR HPV18 OR HPV31 OR HPV33 OR HPV45
L2 1437 SEA ABB=ON PLU=ON L1 AND ("E6" OR "E7")
L3 123 SEA ABB=ON PLU=ON L2 AND ("L1" OR "L2")

FILE 'REGISTRY' ENTERED AT 13:00:30 ON 10 AUG 2000
L4 318 SEA ABB=ON PLU=ON ("INTERLEUKIN-2"? OR "INTERLEUKIN-12"? OR "INTERLEUKIN-7"? OR INTERLEUKIN 2 ? OR INTERLEUKIN 12 ? OR INTERLEUKIN 7 ?)/CN

FILE 'CAPLUS' ENTERED AT 13:00:45 ON 10 AUG 2000
L5 101 SEA ABB=ON PLU=ON L3 AND (TUMOUR OR TUMOR OR NEOPLAS? OR CANCER? OR CARCIN? OR INFECT? OR ANTITUMOR OR ANTITUMOUR OR ANTINEOPLAS? OR ANTICANCER? OR ANTICARCIN? OR ANTIINFECT?)
L6 6 SEA ABB=ON PLU=ON L5 AND (L4 OR IL2 OR IL12 OR IL7 OR (IL OR INTERLEUKIN)(W)(2 OR 12 OR 7) OR IMMUNOSTIMUL? OR IMMUN? STIMUL?)
L7 39 SEA ABB=ON PLU=ON L1 AND (L4 OR IL2 OR IL12 OR IL7 OR (IL OR INTERLEUKIN)(W)(2 OR 12 OR 7) OR IMMUNOSTIMUL? OR IMMUN? STIMUL?)
L8 2 SEA ABB=ON PLU=ON L7 AND (B71 OR B72 OR B7(W)(1 OR 2))

L9 7 SEA ABB=ON PLU=ON L6 OR L8

L9 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:158670 CAPLUS
DOCUMENT NUMBER: 133:57189
TITLE: Human papillomavirus vaccines
AUTHOR(S): Breitburd, Francoise; Coursaget, Pierre
CORPORATE SOURCE: Unite des Papillomavirus, Unite Mixte Institut Pasteur/INSERM U190, Institut Pasteur, Paris, 75015, Fr.
SOURCE: Semin. Cancer Biol. (1999), 9(6), 431-444
CODEN: SECBE7; ISSN: 1044-579X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 99 refs. Genital human papillomavirus (HPV) **infections** are the viral sexually transmitted diseases most frequently diagnosed that include anogenital condylomas and squamous intra-bepithelial lesions, among which the precursors of invasive **carcinomas** of the uterine cervix. In animal PV models, vaccination against **L1** and/or **L2** viral capsid proteins provides an efficient protection against **infection**, involving virus type-specific neutralizing antibodies. Vaccination against non-structural E1, E2, **E6** or

E7 viral proteins does not prevent **infection**, unless administered altogether, but tends to stimulate regression, warranting the design of therapeutic vaccines. Prophylactic vaccines based on the use of virus-like particles (VLPs) obtained by auto-assembly of **L1** or **L1** and **L2** proteins produced by recombinant DNA technol. are under phase I/II clin. trials for HPV6/11 assocd. with condylomas and for **HPV16**, the most frequent oncogenic genotype. Second generation vaccines are chimeric proteins or VLPs incorporating one of the structural proteins (**L1** or **L2**) fused to a non-structural protein (**E6**, **E7** or E2), which should induce both humoral and cellular immunity. Vaccine valency (no. of genotypes), route of administration (humoral vs. local immunity), vaccines (children, young adults, gender) and forms of vaccines (recombinant LSalmonella typhimurium*IL, edible plants expressing **L1** and **L2** proteins, DNA vaccines, synthetic antigenic peptides) are under study. End points to evaluate vaccine efficacy in phase III trials should include viral DNA detection and typing, and screening for low or high grade intraepithelial lesions. Therapeutic vaccines based on recombinant HPV **E6** and/or **E7** vaccinia virus, **L2**-**E7** fusion proteins or **E7** peptides corresponding to cytotoxic T cell epitopes are currently tested (phase I/II trials) in patients with cervical **carcinomas** of advanced clin. stages or high grade intraepithelial lesions. Animal studies, phase I/II clin. trials and implementation of the community support that HPV vaccines will constitute an efficient means to prevent **carcinoma** of the uterine cervix. (c) 1999 Academic Press.

REFERENCE COUNT: 97

REFERENCE(S):
(2) Benyacoub, J; Infec Immun 1999, V67, P3674 CAPLUS
(3) Bergquist, C; Infect Immun 1997, V65, P2676 CAPLUS
(7) Boursnell, M; Vaccine 1996, V14, P1485 CAPLUS
(10) Breitburd, F; J Virol 1995, V69, P3959 CAPLUS
(12) Breitburd, F; Semin Cancer Biol 1996, V7, P359 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:246224 CAPLUS

DOCUMENT NUMBER: 131:86600

TITLE: **Interleukin-12**-secreting human **papillomavirus** type **16**-transformed cells provide a potent cancer vaccine that generates E7-directed immunity

AUTHOR(S): Hallez, Sophie; Detremmerie, Odile; Giannouli,

Searcher : Shears 308-4994

Christina; Thielemans, Kris; Gajewski, Thomas F.; Burny, Arsene; Leo, Oberdan
CORPORATE SOURCE: Laboratoire de Chimie Biologique, Departement de Biologie Moleculaire, Universite Libre de Bruxelles, Rhode-St Genese, 1640, Belg.
SOURCE: Int. J. Cancer (1999), 81(3), 428-437
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The development of a vaccine that would be capable of preventing or curing the (pre)cancerous lesions induced by genital oncogenic human papillomaviruses (HPVs) is the focus of much research. Many studies are presently evaluating vaccines based on the viral E6 and E7 oncoproteins, both of which are continually expressed by tumor cells. The success of a cancer vaccine relies, in large part, on the induction of a tumor-specific ThI-type immunity. In this study, we have evaluated the ability of B7-related and/or **interleukin-12 (IL-12**)-expressing, non-immunogenic murine **HPV16**-transformed BMK-16/myc cells, to achieve this goal. BMK-16/myc cells engineered to express surface **B7-1** or **B7-2** mols. remain tumorigenic in syngeneic BALB/c mice, suggesting that expression of these mols. alone is not sufficient to induce tumor regression. In contrast, mice injected with tumor cells engineered to secrete **IL-12** remained tumor-free, demonstrating that **IL-12** expression is sufficient to induce tumor rejection. **IL-12**-secreting BMK-16/myc cells were further shown to induce potent and specific long-term tumor resistance, even after irradn. **B7-1** was found to slightly but systematically improve anti-tumor immunity elicited by **IL-12**-secreting BMK-16/myc cells. Injection of irradiated B7-I/**IL-12**+ BMK-16/myc cells generates long-lasting, ThI-type, BMK-16/myc-directed immunity in tumor-resistant mice. These mice display a memory-type, E7-specific, cell-mediated immune response, which is potentially significant for clin. applications.
REFERENCE COUNT: 33
REFERENCE(S):
(1) Cavallo, F; J Immunol 1992, V149, P3627 CAPLUS
(2) Cayeux, S; Europ J Immunol 1995, V25, P2325 CAPLUS
(3) Cayeux, S; Hum Gene Ther 1996, V7, P525 CAPLUS
(4) Chen, P; Ann N Y Acad Sci 1996, V795, P325 CAPLUS
(5) Chong, H; Gene Ther 1998, V5, P223 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:77591 CAPLUS
DOCUMENT NUMBER: 130:152552
TITLE: Anti-**tumor** vaccines based on cells presenting **tumor** nuclear antigens on the cell surface
INVENTOR(S): Kieny, Marie-Paule; Balloul, Jean-Marc; Bizouarne, Nadine
PATENT ASSIGNEE(S): Transgene S.A., Fr.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903885	A1	19990128	WO 1998-FR1576	19980717
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2766091	A1	19990122	FR 1997-9152	19970718
AU 9888127	A1	19990210	AU 1998-88127	19980717
EP 989999	A1	20000405	EP 1998-939708	19980717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			FR 1997-9152	19970718
			WO 1998-FR1576	19980717

AB A method of increasing the antigenicity of nuclear antigens by directing them to cell surfaces is described. Redirection is achieved by attaching signal peptides and membrane anchoring domains to the antigen and inactivation of the nuclear localization signal. The method is primarily intended for use in the development of vaccines against human papillomaviruses that play a role in the etiol. of **tumors** of the reproductive tract. The vaccines may be delivered as expression vectors. Genes for a series of derivs. of the **E6** and **E7** proteins of human **papillomavirus 16** carrying signal peptides and transmembrane domains derived from a no. of human and virus proteins were constructed by std. methods. The derivs. also had peptides, such as the binding site for p53 on **E6**, inactivated by mutation. A vaccinia virus carrying modified **E6** and

E7 genes injected into mice was able to induce regression of **tumors** derived from **HPV-16** transformed BMK-**16** cells.

REFERENCE COUNT: 11

REFERENCE(S):
(1) Boursnell, M; Vaccine 1996, V14(16), P1485 CAPLUS
(2) Cancer Res Campaign Tech; WO 9300436 A 1993
(3) Jarrett, W; Nucleic Acids Research 1991, V184, P33 CAPLUS
(4) Meneguzzi, G; Journal of Cellular Biochemistry Part C 1989, Sup 13, P210
(5) Seedorf, K; Virology 1985, V145(1), P181 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:106018 CAPLUS
DOCUMENT NUMBER: 128:179355
TITLE: Papillomavirus vaccines using early and late proteins as antigens
INVENTOR(S): Balloul, Jean-Marc; Bizouarne, Nadine; Kieny, Marie-Paule
PATENT ASSIGNEE(S): Transgene S.A., Fr.; Balloul, Jean-Marc; Bizouarne, Nadine; Kieny, Marie-Paule
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804705	A1	19980205	WO 1997-FR1412	19970729
W: AU, CA, JP, SG, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2751879	A1	19980206	FR 1996-9584	19960730
FR 2751879	B1	19981030		
CA 2234263	AA	19980205	CA 1997-2234263	19970729
AU 9738552	A1	19980220	AU 1997-38552	19970729
EP 862634	A1	19980909	EP 1997-935646	19970729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000500662	T2	20000125	JP 1998-508568	19970729
PRIORITY APPLN. INFO.:			FR 1996-9584	19960730
			WO 1997-FR1412	19970729

AB Vaccines for prevention or treatment of papillomavirus **infection** or **tumor** using early and late viral

proteins as antigens. The antigens may be used in combination with **immunostimulatory** peptides. Vector vaccines using genes for these antigens may also be used. Construction of vaccinia virus expression vectors for antigen genes of **HPV-16** and interleukins is described. The genes were inserted into the K1L region and TK regions. The p7.5K and pH5R promoters were used to drive expression of the genes. Two of these vaccinia virus vectors did not cause any ill effects in nude mice upon either intracranial or i.v. injection. Mice inoculated three times with 107 pfu of virus were subsequently challenged with 103 cells of a cell line transformed with the **E7** oncogene of **HPV16**. All of the control animals were dead 36 days after challenge. At the same point, 40% of the inoculated animals had survived and 30% survived to 51 days.

L9 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:681541 CAPLUS
DOCUMENT NUMBER: 125:309006
TITLE: Treatment of papillomavirus-associated lesions using **interleukin-12**
INVENTOR(S): Stanley, Margaret Anne; Scarpini, Cinzia Giuseppina
PATENT ASSIGNEE(S): Cambridge University Technical Services Limited, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629091	A1	19960926	WO 1996-GB686	19960322
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2215525	AA	19960926	CA 1996-2215525	19960322
AU 9651515	A1	19961008	AU 1996-51515	19960322
EP 817644	A1	19980114	EP 1996-908184	19960322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11502813	T2	19990309	JP 1996-528209	19960322
US 6096869	A	20000801	US 1996-621841	19960322
PRIORITY APPLN. INFO.:			GB 1995-5784	19950322
			WO 1996-GB686	19960322

AB **Interleukin-12** (**IL-12**) or a functional analog thereof, or a polynucleotide encoding **IL-12** or encoding a functional analog thereof, is used as a

therapeutic material or adjuvant in treating papillomavirus-assocd. lesions e.g. warts due to HPV 6 and/or 11, e.g. condyloma acuminata. **IL-12** or a vector encoding it for endogenous prodn. can be used together with a vaccine such as a papillomavirus antigen, or a vector encoding a papillomavirus antigen. A role of **IL-12** in wart regression and a link between dendritic cell expression of **IL-12** and wart regression are described. **IL-12** enhanced the immune response in an in vivo model (mouse keratinocytes expressing HPV **E6** or **E7** grafted in syngeneic mice), as evidenced by a delayed type hypersensitivity reaction.

L9 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:616379 CAPLUS
DOCUMENT NUMBER: 125:238677
TITLE: Human papillomavirus proteins as **immunostimulants** and vaccines, especially gene **L2-E7** fusion protein recombinant production and wart treatment
INVENTOR(S): Whittle, Nigel Richard; Carmichael, Jeremy Paddon; Connor, Stephen Edward; Thompson, Henry Stephen Grammer; Wilson, Mark Jonathan
PATENT ASSIGNEE(S): Cantab Pharmaceuticals Research Limited, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9626277	A1	19960829	WO 1996-GB397	19960223
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2211995	AA	19960829	CA 1996-2211995	19960223
AU 9647272	A1	19960911	AU 1996-47272	19960223
EP 812358	A1	19971217	EP 1996-903127	19960223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11501804	T2	19990216	JP 1996-525496	19960223
US 5955087	A	19990921	US 1996-606288	19960223
AU 9944544	A1	19991021	AU 1999-44544	19990817

PRIORITY APPLN. INFO.: GB 1995-3786 19950224
US 1995-34 19950608
GB 1995-15478 19950728
AU 1996-47272 19960223

Searcher : Shears 308-4994

WO 1996-GB397 19960223

AB Fusion polypeptides and aggregates of polypeptides comprising papillomavirus-derived antigens, and compns. thereof and their use e.g. with adjuvants for immunogenic and vaccine purposes in eliciting e.g. HPV-specific immune responses. The polypeptides can be purified to result in aggregates which when in soln. or dispersion can pass through a sterilization filter, and in amorphous aggregates. An example of such a polypeptide is a fusion protein of human papillomavirus proteins **L2** and **E7**.

L9 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:483722 CAPLUS
DOCUMENT NUMBER: 125:140546
TITLE: Induction of cytotoxic T-lymphocyte responses
INVENTOR(S): Raychaudhuri, Syamal; Rastetter, William H.
PATENT ASSIGNEE(S): Idec Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9617863	A1	19960613	WO 1995-US15433	19951129
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5709860	A	19980120	US 1994-351001	19941207
AU 9644104	A1	19960626	AU 1996-44104	19951129
AU 699044	B2	19981119		
EP 801656	A1	19971022	EP 1995-942921	19951129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
BR 9509872	A	19971125	BR 1995-9872	19951129
JP 10510264	T2	19981006	JP 1995-517641	19951129
NO 9702521	A	19970806	NO 1997-2521	19970603
FI 9702431	A	19970606	FI 1997-2431	19970606
PRIORITY APPLN. INFO.:			US 1994-351001	19941207
			US 1991-735069	19910725
			US 1992-919787	19920724
			WO 1995-US15433	19951129

AB Methods and compns. useful for inducing a cytotoxic T-lymphocyte response (CTL) in a human or domesticated or agriculturally

important animal. The method includes the steps of providing the antigen to which the CTL response is desired and providing an antigen formulation which comprises, consists, or consists essentially of two or more of a stabilizing detergent, a micelle-forming agent, and an oil. This antigen formulation is preferably lacking in an **immunostimulating** peptide component, or has sufficiently low levels of such a component that the desired CTL response is not diminished. This formulation is provided as a stable oil-in-water emulsion.

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 13:11:01 ON 10 AUG 2000)
L10 12 S L9
L11 7 DUP REM L10 (5 DUPLICATES REMOVED)

L11 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:228303 BIOSIS
DOCUMENT NUMBER: PREV200000228303
TITLE: Human dendritic cells infected with an avipox recombinant encoding a triad of human costimulatory molecules enhances the induction of antigen specific T-cell responses.
AUTHOR(S): Zhu, M. Z. (1); Terasawa, H.; Arlen, P.; Panicali, D.; Schlom, J.; Tsang, K. Y.
CORPORATE SOURCE: (1) National Cancer Inst, Bethesda, MD USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 218.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L11 ANSWER 2 OF 7 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999224664 MEDLINE
DOCUMENT NUMBER: 99224664
TITLE: **Interleukin-12**-secreting human **papillomavirus** type **16**-transformed cells provide a potent cancer vaccine that generates E7-directed immunity.
AUTHOR: Hallez S; Detremmerie O; Giannouli C; Thielemans K; Gajewski T F; Burny A; Leo O
CORPORATE SOURCE: Departement de Biologie Moleculaire, Universite Libre de Bruxelles, Rhode-St Gen`ese, Belgium.. shallez@dbm.ulb.ac.be
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1999 May 5) 81 (3)

428-37.
Journal code: GQU. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990701

AB The development of a vaccine that would be capable of preventing or curing the (pre)cancerous lesions induced by genital oncogenic human papillomaviruses (HPVs) is the focus of much research. Many studies are presently evaluating vaccines based on the viral E6 and E7 oncoproteins, both of which are continually expressed by tumor cells. The success of a cancer vaccine relies, in large part, on the induction of a tumor-specific Th1-type immunity. In this study, we have evaluated the ability of B7-related and/or **interleukin -12 (IL-12)**-expressing, non-immunogenic murine **HPV16**-transformed BMK-16/myc cells, to achieve this goal. BMK-16/myc cells engineered to express surface **B7-1** or **B7-2** molecules remain tumorigenic in syngeneic BALB/c mice, suggesting that expression of these molecules alone is not sufficient to induce tumor regression. In contrast, mice injected with tumor cells engineered to secrete **IL-12** remained tumor-free, demonstrating that **IL-12** expression is sufficient to induce tumor rejection. **IL-12**-secreting BMK-16/myc cells were further shown to induce potent and specific long-term tumor resistance, even after irradiation. **B7-1** was found to slightly but systematically improve anti-tumor immunity elicited by **IL-12**-secreting BMK-16/myc cells. Injection of irradiated **B7-1/IL-12**+ BMK-16/myc cells generates long-lasting, Th1-type, BMK-16/myc-directed immunity in tumor-resistant mice. These mice display a memory-type, E7-specific, cell-mediated immune response, which is potentially significant for clinical applications.

L11 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:354989 BIOSIS
DOCUMENT NUMBER: PREV199900354989
TITLE: Human **papillomavirus 16** E7-specific CTL induction through mouse **B7-1** costimulating with E7C subgene.
AUTHOR(S): Xu, Jianqing (1); Si, Jingyi (1); Zhang, Youhui (1)
CORPORATE SOURCE: (1) Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, 100005 China
SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi, (May, 1999) Vol. 19, No. 3, pp. 227-231.
ISSN: 0254-5101.
DOCUMENT TYPE: Article

LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English
AB Objectives To develop a prophylactic and therapeutic vaccine against **HPV16** with the E7C subgene possessing the antigenicity of E7 and no transformational activity, and trying to explore more active vaccine for inducing cellular immunity with **B7-1** . Methods In these experiments, the E7C was amplified by PCR and then inserted into eukaryotic expression plasmid for constructing pLNCE7C. Being confirmed the ability to express in eukaryotic cells in vitro, the pLNCE7C plasmid alone or associated with mouse **B7-1** was inoculated directly into the muscles on the posterior leg of C57BL/6 mice, the activity of cytotoxic T lymphocytes (CTL) isolated from the immunized mice were analyzed in vitro with 51Cr specific release assay. Results The CTLs from immunized mice were activated efficaciously by naked E7-expression plasmid; higher activity of CTL could be produced by **B7-1** synergizing with E7C through immunizing with the mixture of both expressing plasmids. Conclusions E7C subgene is proved suitable for developing DNA vaccine, and the **B7-1** is worthy for exploiting widely.

L11 ANSWER 4 OF 7 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 1999:11232 SCISEARCH
THE GENUINE ARTICLE: 148GN
TITLE: Construction and characterization of a triple-recombinant vaccinia virus encoding **B7-1, interleukin** 12, and a model tumor antigen
AUTHOR: Carroll M W; Overwijk W W; Surman D R; Tsung K; Moss B; Restifo N P (Reprint)
CORPORATE SOURCE: NCI, DIV CLIN SCI, SURG BRANCH, NIH, BLDG 10, RM 2B42, BETHESDA, MD 20892 (Reprint); NCI, DIV CLIN SCI, SURG BRANCH, NIH, BETHESDA, MD 20892; NIAID, VIRAL DIS LAB, NIH, BETHESDA, MD 20892; WASHINGTON UNIV, DEPT SURG, ST LOUIS, MO
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (16 DEC 1998) Vol. 90, No. 24, pp. 1881-1887. Publisher: NATL CANCER INSTITUTE, 9030 OLD GEORGETOWN RD, BETHESDA, MD 20814. ISSN: 0027-8874.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Construction of recombinant viruses that can serve as vaccines for the treatment of experimental murine tumors has recently been achieved, The cooperative effects of immune system

modulators, including cytokines such as **interleukin 12 (IL-12)** and costimulatory molecules such as **B7-1**, may be necessary for activation of cytotoxic T lymphocytes, Thus, we have explored the feasibility and the efficacy of inclusion of these immunomodulatory molecules in recombinant virus vaccines in an experimental antitumor model in mice that uses Escherichia coli P-galactosidase as a target antigen. Methods: We developed a ''cassette'' system in which three loci of the vaccinia virus genome were used for homologous recombination, A variety of recombinant vaccinia viruses were constructed, including one virus, vB7/beta/ **IL-12**, that contains the following five transgenes: murine **B7-1**, murine **IL-12** subunit p35, murine **IL-12** subunit p40, E, coli lacZ (encodes P-galactosidase, the model antigen), and E, coli gpt (xanthine-guanine phosphoribosyltransferase, a selection gene). The effects of the recombinant viruses on lung metastases and survival were tested in animals that had been given an intravenous injection of beta-galactosidase-expressing murine colon carcinoma cells 3 days before they received the recombinant virus by intravenous inoculation. Results: Expression of functional **B7-1** and **IL-12** by virally infected cells was demonstrated ia vitro. Lung tumor nodules (i,e,, metastases) were reduced in mice by more than 95% after treatment with the virus vB7/beta/**IL-12**; a further reduction in lung tumor nodules was observed when exogenous **IL-12** was also given. Greatest survival of tumor-bearing mice was observed in those treated with viruses encoding P-galactosidase and **B7-1** plus exogenous **IL-12**, Conclusion: This study shows the feasibility of constructing vaccinia viruses that express tumor antigens and multiple immune cofactors to create unique immunologic microenvironments that can modulate immune responses to cancer.

L11 ANSWER 5 OF 7 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 97:322565 SCISEARCH
THE GENUINE ARTICLE: WU896
TITLE: Cell mediated immunity induced in mice by **HPV 16 L1** virus-like particles
AUTHOR: Dupuy C; BuzoniGatel D; Touze A; LeCann P; Bout D; Coursaget P (Reprint)
CORPORATE SOURCE: FAC PHARM TOURS, LAB IMMUNOL MALAD INFECT, 31 AVE MONGE, F-37200 TOURS, FRANCE (Reprint); FAC PHARM TOURS, LAB IMMUNOL MALAD INFECT, F-37200 TOURS, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: MICROBIAL PATHOGENESIS, (APR 1997) Vol. 22, No. 4, pp. 219-225.

Searcher : Shears 308-4994

Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON, ENGLAND NW1 7DX.
ISSN: 0882-4010.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recombinant human **papillomavirus** (**HPV**) type **16** **L1** virus-like particles (VLPs) expressed in the baculovirus system were used to investigate the cellular immune response to human **papillomavirus** type **16**. The cell-mediated immune response was evaluated through immunization of mice with **HPV** **16** **L1** virus-like particles using a lymphoproliferation assay and cytokine production and cytometric analysis of lymphocyte subsets. A significant proliferative response was observed which was associated with secretion of both interferon-gamma and **interleukin-2**. FAGS analysis of splenic lymphocytes revealed that CD8(+) T-cells were increased in the immunized mice. These results demonstrate that **HPV** **16** **L1** VLPs induce a T-cell response characterized by a Th1 profile and confirm that the **HPV** **16** VLP is a reasonable candidate for vaccine development. (C) 1997 Academic Press Limited.

L11 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 2000 ISI (R)

ACCESSION NUMBER: 95:180275 SCISEARCH
THE GENUINE ARTICLE: QL084

TITLE: ANTITUMOR IMMUNITY ELICITED BY TUMOR-CELLS TRANSFECTED WITH **B7-2**, A 2ND LIGAND FOR CD28/CTLA-4 COSTIMULATORY MOLECULES

AUTHOR: YANG G C; HELLSTROM K E; HELLSTROM I; CHEN L P (Reprint)
CORPORATE SOURCE: BRISTOL MYERS SQUIBB PHARMACEUT RES INST, 3005 1ST AVE, SEATTLE, WA, 98121 (Reprint); BRISTOL MYERS SQUIBB PHARMACEUT RES INST, SEATTLE, WA, 98121
COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF IMMUNOLOGY, (15 MAR 1995) Vol. 154, No. 6, pp. 2794-2800.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have examined the role of the **B7-2** costimulatory molecule, a second ligand for CD28/CTLA-4 counterreceptors, in the induction of antitumor immunity. A plasmid containing murine **B7-2** cDNA was transfected into

the immunogenic mouse mastocytoma P815 of DBA/2 origin. In contrast to the lethal growth of the wild-type (wt) P815 tumor, **B7-2**-positive (**B7-2**(+)) P815 cells inoculated into syngeneic mice regressed, and immunization of mice with such tumor cells protected them against the challenge of wt P815 tumor. Depletion of CD8(+), but not of CD4(+), lymphocytes in vivo by specific Abs abolished the regression of **B7-2**(+) P815 tumors. CD8(+) cytolytic T cells could be generated from mice immunized with **B7-2**(+) P815. They were found to be MHC class I-restricted and specific for the P815 tumor. In contrast, transfection of the **B7-2** gene into the nonimmunogenic MCA102 fibrosarcoma of C57BL/6 origin induced neither tumor regression nor protective immunity. Co-expression on MCA102 cells of **B7-2** together with the related costimulator **B7-1** also failed to induce immunity to MCA102 tumor. Our results indicate that transfection of **B7-2** into tumor cells can improve host response to some tumors, and that the effects seen are similar to those previously observed for **B7-1**.

L11 ANSWER 7 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95210573 EMBASE
DOCUMENT NUMBER: 1995210573
TITLE: Human papillomavirus in vulvar and vaginal **carcinoma** cell lines.
AUTHOR: Hietanen S.; Grenman S.; Syrjanen K.; Lappalainen K.; Kauppinen J.; Carey T.; Syrjanen S.
CORPORATE SOURCE: Medicity Research Laboratory, Turku University, Tykistokatu 6,20520 Turku, Finland
SOURCE: British Journal of Cancer, (1995) 72/1 (134-139). ISSN: 0007-0920 CODEN: BJCAAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology
016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A number of reports associate human papillomavirus (HPV) with cervical **cancer** and **cancer** cell lines derived from this **tumour** type. Considerably fewer reports have focused on the role of HPV in **carcinomas** from other sites of female anogenital squamous epithelia. In this study we have tested for the presence of HPV in eight low-passage vulvar **carcinoma** cell lines and one extensively passaged cell line, A431. One cell line from a primary vaginal **carcinoma** was included. The presence of the HPV was evaluated by the polymerase chain reaction (PCR), by Southern blot analysis and by two

dimensional gel electrophoresis. General primer-mediated PCR was applied by using primers from the **L1** region, E1 region and **HPV 16 E7** region. Southern blot hybridisation was performed under low-stringency conditions (T(m) = -35.degree.C) using a whole genomic **HPV** 6/**16**/**18** probe mixture and under high stringency conditions (T(m) = -18.degree.C) with the whole genomic probes of **HPV 16** and **33**. **HPV 16 E6**-**E7** mRNA was assessed by ribonuclease protection assay (RPA). HPV was found in only one vulvar **carcinoma** cell line, UM-SCV-6. The identified type, **HPV 16**, was integrated in the cell genome and could be amplified with all primers used. Also **E6**-**E7** transcripts were found in these cells. Five original **tumour** biopsies were available from the HPV-negative cell lines for in situ hybridisation. All these were HPV negative with both the **HPV** 6/**16**/**18** screening probe mixture under low stringency and the **HPV 16** probe under high stringency. The results indicate that vulvar **carcinoma** cell lines contain HPV less frequently than cervical **carcinoma** cell lines and suggest that a significant proportion of vulvar **carcinomas** may evolve by an HPV-independent mechanism.

FILE 'CAPLUS' ENTERED AT 13:24:38 ON 10 AUG 2000

L12 11 S L3 AND DYSPLAS?

L14 1 SEA ABB=ON PLU=ON L12 AND (L4 OR IL2 OR IL12 OR IL7 OR (IL OR INTERLEUKIN)(W)(2 OR 12 OR 7) OR IMMUNOSTIMUL? OR IMMUN? STIMUL?)

L15 0 SEA ABB=ON PLU=ON L14 NOT L9

FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 13:26:36 ON 10 AUG 2000

L16 0 SEA ABB=ON PLU=ON L14

(FILE 'MEDLINE' ENTERED AT 13:32:21 ON 10 AUG 2000)

L17 4253 SEA FILE=MEDLINE ABB=ON PLU=ON "PAPILLOMAVIRUS, HUMAN"/CT

L18 23429 SEA FILE=MEDLINE ABB=ON PLU=ON INTERLEUKIN-2/CT

L19 775 SEA FILE=MEDLINE ABB=ON PLU=ON INTERLEUKIN-7/CT

L20 2593 SEA FILE=MEDLINE ABB=ON PLU=ON INTERLEUKIN-12/CT

L21 16 SEA FILE=MEDLINE ABB=ON PLU=ON L17 AND (L18 OR L19 OR L20)

L21 ANSWER 1 OF 16 MEDLINE

AN 2000240058 MEDLINE

TI Interleukin-10 increases Th1 cytokine production and cytotoxic potential in human papillomavirus-specific CD8(+) cytotoxic T

lymphocytes.

AU Santin A D; Hermonat P L; Ravaggi A; Bellone S; Pecorelli S; Roman J J; Parham G P; Cannon M J

SO JOURNAL OF VIROLOGY, (2000 May) 74 (10) 4729-37.
Journal code: KCV. ISSN: 0022-538X.

AB Interleukin-10 (IL-10) is widely known as an immunosuppressive cytokine by virtue of its ability to inhibit macrophage-dependent antigen presentation, T-cell proliferation, and Th1 cytokine secretion. However, several studies have challenged the perception of IL-10 solely as an immunosuppressive cytokine. As part of an investigation on potentiation of the cytotoxic activity of human papillomavirus E7-specific CD8(+) cytotoxic T lymphocytes (CTL) for adoptive transfusions to cervical cancer patients, we found that IL-10 in combination with IL-2, unlike several other combinations, including IL-2 with IL-12, gamma interferon (IFN-gamma), tumor necrosis factor alpha, and transforming growth factor beta, was able to consistently increase cytotoxicity. This augmentation in cytotoxic activity correlated with a significant increase in the cytoplasmic accumulation of perforin as detected by fluorescence-activated cell sorter. Surface expression of both the alpha and beta chains of the CD8 heterodimeric coreceptor and CD56 molecules was increased by exposure of CTL to IL-10. More importantly, we found that administration of IL-10 in combination with IL-2 after antigen stimulation consistently increased the intracellular expression of Th1 cytokines (i.e., IFN-gamma and IL-2) compared to results for control CD8(+) T cells cultured in IL-2 alone. In kinetic studies, proliferation, intracellular perforin levels, cytotoxic activity, and IFN-gamma expression were consistently elevated in CTL cultures containing IL-10 compared to control cultures, both at early and late time points following stimulation. In contrast, intracellular IL-2 expression was consistently increased only at early time points following stimulation with autologous tumor cells or solid-phase anti-CD3 antibody. Taken together, these data support the use of IL-10 in combination with IL-2 for the in vitro expansion and potentiation of tumor-specific CTL for clinical use in the therapy of cancer.

L21 ANSWER 2 OF 16 MEDLINE

AN 2000187653 MEDLINE

TI Cytokine profile in genital tract secretions from female adolescents: impact of human immunodeficiency virus, human papillomavirus, and other sexually transmitted pathogens.

AU Crowley-Nowick P A; Ellenberg J H; Vermund S H; Douglas S D; Holland C A; Moscicki A B

SO JOURNAL OF INFECTIOUS DISEASES, (2000 Mar) 181 (3) 939-45.
Journal code: IH3. ISSN: 0022-1899.

AB Quantitative enzyme-linked immunosorbent assays were used to measure interleukin (IL)-2, IL-10, and IL-12 in cervical secretions from female adolescents with and without sexually transmitted infections.

Compared with human immunodeficiency virus [HIV]-negative patients, HIV-positive patients had higher concentrations of IL-10 (118.2 pg/mL vs. 34.5 pg/mL; P=.002) and IL-12 (175.5 pg/mL vs. 85.1; P=.03). IL-2 concentrations were not statistically different. Furthermore, genital tract infections were predictors of IL-10 and IL-12 concentrations. Coinfection with HIV and human papillomavirus predicted the highest IL-10 concentrations; coinfection with HIV, human papillomavirus, and other sexually transmitted pathogens predicted the highest IL-12 concentrations. The data indicate that concomitant infection of the genital tract with HIV and other viral, bacterial, or protozoan pathogens influences the local concentrations of some immunoregulatory cytokines.

L21 ANSWER 3 OF 16 MEDLINE
AN 1999429609 MEDLINE
TI Human papillomavirus type 16 E2-specific T-helper lymphocyte responses in patients with cervical intraepithelial neoplasia.
AU Bontkes H J; de Gruijl T D; Bijl A; Verheijen R H; Meijer C J; Scheper R J; Stern P L; Burns J E; Maitland N J; Walboomers J M
SO JOURNAL OF GENERAL VIROLOGY, (1999 Sep) 80 (Pt 9) 2453-9. Journal code: I9B. ISSN: 0022-1317.
AB T-cell-mediated immune responses against mucosal oncogenic types of human papillomaviruses (HPV) are thought to play a role in the control of the virus infection and its associated cervical lesions. The in vitro production of interleukin-2 by T-helper (Th) cells in response to the C-terminal and N-terminal domains of the HPV-16 E2 protein was determined in 74 women with cytological evidence of premalignant cervical epithelial neoplasia who participated in a non-intervention follow-up (FU) study. Cross-sectional analysis at the end of FU showed that Th cell responses against the C-terminal domain were associated with evidence of previous or present HPV-16 infection as compared to patients with no evidence of any HPV infection (18.9% versus 0%, P = 0.039). Th cell responses against the N-terminal domain were not associated with evidence of HPV-16 infection. No association with disease outcome was observed with Th cell responses against either of the E2 protein domains. However, longitudinal analysis revealed that Th cell responses against the C-terminal domain frequently occur at the time of virus clearance. Whether these responses are responsible for the clearance of the virus is not known.

L21 ANSWER 4 OF 16 MEDLINE
AN 1999224664 MEDLINE
TI Interleukin-12-secreting human papillomavirus type 16-transformed cells provide a potent cancer vaccine that generates E7-directed immunity.
AU Hallez S; Detremmerie O; Giannouli C; Thielemans K; Gajewski T F; Burny A; Leo O
SO INTERNATIONAL JOURNAL OF CANCER, (1999 May 5) 81 (3) 428-37.

Journal code: GQU. ISSN: 0020-7136.

AB The development of a vaccine that would be capable of preventing or curing the (pre)cancerous lesions induced by genital oncogenic human papillomaviruses (HPVs) is the focus of much research. Many studies are presently evaluating vaccines based on the viral E6 and E7 oncoproteins, both of which are continually expressed by tumor cells. The success of a cancer vaccine relies, in large part, on the induction of a tumor-specific Th1-type immunity. In this study, we have evaluated the ability of B7-related and/or interleukin-12 (IL-12)-expressing, non-immunogenic murine HPV16-transformed BMK-16/myc cells, to achieve this goal. BMK-16/myc cells engineered to express surface B7-1 or B7-2 molecules remain tumorigenic in syngeneic BALB/c mice, suggesting that expression of these molecules alone is not sufficient to induce tumor regression. In contrast, mice injected with tumor cells engineered to secrete IL-12 remained tumor-free, demonstrating that IL-12 expression is sufficient to induce tumor rejection. IL-12-secreting BMK-16/myc cells were further shown to induce potent and specific long-term tumor resistance, even after irradiation. B7-1 was found to slightly but systematically improve anti-tumor immunity elicited by IL-12-secreting BMK-16/myc cells. Injection of irradiated B7-1/IL-12+ BMK-16/myc cells generates long-lasting, Th1-type, BMK-16/myc-directed immunity in tumor-resistant mice. These mice display a memory-type, E7-specific, cell-mediated immune response, which is potentially significant for clinical applications.

L21 ANSWER 5 OF 16 MEDLINE

AN 1999171708 MEDLINE

TI Immune responses against human papillomavirus (HPV) type 16 virus-like particles in a cohort study of women with cervical intraepithelial neoplasia. I. Differential T-helper and IgG responses in relation to HPV infection and disease outcome.

AU de Gruijl T D; Bontkes H J; Walboomers J M; Coursaget P; Stukart M J; Dupuy C; Kueter E; Verheijen R H; Helmerhorst T J; Duggan-Keen M F; Stern P L; Meijer C J; Scheper R J

SO JOURNAL OF GENERAL VIROLOGY, (1999 Feb) 80 (Pt 2) 399-408. Journal code: I9B. ISSN: 0022-1317.

AB T-helper (Th) cell-dependent IL-2 production and plasma IgG responses to virus-like particles consisting of the human papillomavirus type 16 (HPV-16) major capsid protein L1 (L1-VLP) were determined in patients with cytological evidence of cervical intraepithelial neoplasia (CIN) participating in a non-intervention prospective cohort study. IgG responses were associated with HPV-16 persistence and high-grade CIN lesions, while high frequencies of Th responses were observed in patients with both virus clearance and virus persistence, irrespective of CIN grade. The IgG response was found in conjunction with an IL-2 response to L1-VLP in 87% of the patients. Recognition of the HPV-16 L1 Th epitope (amino acids 311-335) was found to be more closely associated than recognition of

L1-VLP as a whole to HPV exposure and CIN development. Among the HPV-16+ patients included in this study, those showing a Th response to amino acids 311-335 were more likely to carry the HLA DRB1*11/DQB1*0301 haplotype, while those showing an IgG response to L1-VLP were more likely to carry DRB1*0101/DQB1*0501. However, neither cell-mediated nor humoral immune responses against HPV-16 L1 appear to be sufficient for the natural control of HPV infection and CIN development.

L21 ANSWER 6 OF 16 MEDLINE
AN 1999150474 MEDLINE
TI Interleukin 2 gene therapy of residual disease in mice carrying tumours induced by HPV 16.
AU Bubenik J; Simova J; Hajkova R; Sobota V; Jandlova T; Smahel M; Sobotkova E; Vonka V
SO INTERNATIONAL JOURNAL OF ONCOLOGY, (1999 Mar) 14 (3) 593-7. Journal code: CX5. ISSN: 1019-6439.
AB Experiments were designed to examine the efficacy of IL-2 gene therapy in a surgical minimal residual tumour disease, using moderately immunogenic MK16/1/IIIABC murine cells transformed by activated ras and HPV 16 E6/E7 oncogenes (MK16 cells). Previously we demonstrated that surgical minimal residual tumour disease (SMRTD) could be effectively cured when murine Mc12 sarcoma had been resected and the operated mice were treated with irradiated Mc12 sarcoma cells engineered to secrete IL-2. In this study we performed IL-2 gene therapy of MK16 carcinoma with two types of irradiated MK16-unrelated tumour cell vaccines. One type of vaccine was derived from MHC class I-matched Mc12 sarcoma cells engineered to secrete IL-2 and the other from MHC class I-discordant IL-2 producing plasmacytoma X63-m-IL-2. The vaccines did not share any tumour rejection antigen with the MK16 cells and served exclusively as a local source of IL-2 production. Both vaccines were capable of inhibiting MK16 tumours when administered peritumorally up to 15 days after MK16 tumour challenge. The irradiated MHC class I-matched and IL-2-producing Mc12 sarcoma vaccine was then selected for therapy of MK16 SMRTD. Whereas the recurrence rate in the operated MK16 carcinoma bearers was 80%, so that only 20% of mice were cured by surgery, approximately 65% of the MK16 carcinoma bearers were permanently protected when the surgery was followed by local administration of the IL-2-producing Mc12 sarcoma vaccine.

L21 ANSWER 7 OF 16 MEDLINE
AN 1999129160 MEDLINE
TI Potentiation of E7 antisense RNA-induced antitumor immunity by co-delivery of IL-12 gene in HPV16 DNA-positive mouse tumor.
AU He Y K; Lui V W; Baar J; Wang L; Shurin M; Almonte C; Watkins S C; Huang L
SO GENE THERAPY, (1998 Nov) 5 (11) 1462-71. Journal code: CCE. ISSN: 0969-7128.

AB Down-regulation of oncogene expression by antisense-based gene therapy has been extensively studied, and in some cases, therapeutic effects have been demonstrated. We have previously shown that down-regulation of HPV16 E6 and E7 gene expression inhibited HPV DNA-positive C3 mouse tumor growth. Although not all of the tumor cells were transfected by pU6E7AS plasmid, complete tumor regression was achieved if the tumor size was small at the start of therapy in a syngeneic host. This suggests that some other antitumor mechanisms may be involved in addition to the direct down-regulation of HPV16 E7 oncogene expression by the antisense effect of E7AS. In the current study, we demonstrated that E7AS induces tumor cell apoptosis. More importantly, a strong antitumor immune response was elicited in the pU6E7AS-treated and tumor-regressed mice. There was no tumor growth after rechallenging the tumor-regressed mice with 1 million C3 cells. This E7AS-induced antitumor immune response was augmented by co-delivery of mIL-12 cytokine gene. The combination therapy strategy resulted in complete regression of 26 of 28 (93%) tumors. Only 12 of 31 (38%) tumors from the group treated with pU6E7AS alone and 14 of 28 (50%) tumors from the group treated with pCMVmIL-12 alone had completely regressed. Complete regression was also demonstrated in tumors located 1 cm from the treated tumors, which indicates that a systemic antitumor effect was induced by E7AS and mIL-12. Immunohistochemistry demonstrated that a significant amount of CD4+ and CD8+ cells infiltrated into tumors treated with pU6E7AS, pCMVmIL-12 and pU6E7AS+pCMVmIL-12. These data indicate that host immunity is an important factor for antisense-based gene therapy approach which can be further enhanced by combination with cytokine gene therapy.

L21 ANSWER 8 OF 16 MEDLINE
AN 1999115242 MEDLINE
TI Differential expression of immunobiological mediators by immortalized human cervical and vaginal epithelial cells.
AU Fichorova R N; Anderson D J
SO BIOLOGY OF REPRODUCTION, (1999 Feb) 60 (2) 508-14.
Journal code: A3W. ISSN: 0006-3363.
AB We have recently generated human papillomavirus (HPV) 16/E6E7 immortalized epithelial cell lines from the human vagina, ectocervix, and endocervix to use in studies on the role of these cells in reproduction and immune defense. The cell lines maintain the differentiation characteristics of their tissues of origin: the endocervical cell line expresses characteristics of simple columnar epithelium, whereas the ectocervical and vaginal cell lines express characteristics of stratified squamous nonkeratinizing epithelia. As a first step in elucidating the role of these cells in immune defense, we have studied the expression of immunological mediators in nonstimulated and stimulated cultures. Without stimulation, all three lines consistently produced the cytokines macrophage colony-stimulating factor (M-CSF) and transforming growth factor

beta1, the chemokine interleukin (IL)-8, prostaglandin E2, the secretory leukoproteinase inhibitor, and the polymeric immunoglobulin receptor. The endocervical cell line, but not the others, also produced the lymphopoietic cytokines IL-6, IL-7, and consistently detectable levels of the chemokine known as "regulated-upon-activation, normal T cell expressed and secreted" (RANTES). Stimulation with the exogenous cytokines interferon gamma and tumor necrosis factor alpha induced or significantly up-regulated expression of several of the cytokines and chemokines (i.e., IL-6, IL-8, RANTES, and M-CSF), as well as major histocompatibility complex (MHC) class II antigens, and membrane expression and shedding of the intercellular adhesion molecule-1 in all three cell lines. These data provide further evidence that epithelial cells in the lower human female genital tract participate in immunological functions, that their activity is up-regulated by proinflammatory/immune cytokines, and that epithelial cell immunological functions vary at different anatomical sites in the genital tract.

L21 ANSWER 9 OF 16 MEDLINE
AN 1999079618 MEDLINE
TI HPV and intraepithelial neoplasia recurrent lesions of the lower genital tract: assessment of the immune system.
AU Stentella P; Frega A; Ciccarone M; Cipriano L; Tinari A; Tzantzoglou S; Pach`i A
SO EUROPEAN JOURNAL OF GYNAECOLOGICAL ONCOLOGY, (1998) 19 (5) 466-9. Journal code: ENA. ISSN: 0392-2936.
AB OBJECTIVE: To evaluate the immune state in patients with genital relapse HPV and intraepithelial lesions of the lower genital tract. METHOD: Forty-three patients were selected. Twenty-one were affected by recurrent HPV infection either alone or combined with intraepithelial neoplasia treated by laser surgery, and 22 had been previously-treated and clinically cured without recurrence during a follow-up from 18 to 24 months. The diagnostic protocol included colposcopy with eso- and endocervical cytology histologically confirmed by directed biopsy. Afterwards patients underwent a systemic immunogenic evaluation. RESULTS: NK cell reduction was strictly related to HPV infection associated with intraepithelial lesions; B-lymphocyte reduction was percentually greater in patients affected by HPV alone; activation of R-IL2 increased in a percentage overlapping in the two groups indicating patient reaction to the virus. CONCLUSION: Our study supports the theory that immune response directed against viral antigens is one of the most important effectors in the control of HPV infections and that HPV is the cause of a systemic rather than local lesion.

L21 ANSWER 10 OF 16 MEDLINE
AN 1998276520 MEDLINE
TI Correlation of T-helper secretory differentiation and types of

antigen-presenting cells in squamous intraepithelial lesions of the uterine cervix.

AU al-Saleh W; Giannini S L; Jacobs N; Moutschen M; Doyen J; Boniver J; Delvenne P

SO JOURNAL OF PATHOLOGY, (1998 Mar) 184 (3) 283-90.
Journal code: JLB. ISSN: 0022-3417.

AB This study addressed the notion that the progression of cervical cancer is associated with a T-helper 2 (TH2) immunodeviation by analysing cytokine expression in 60 cervical biopsy specimens, spanning the spectrum from normal cervical tissue to high-grade squamous intraepithelial lesions (SILs). The biopsies were analysed by immunohistochemistry for the expression of TH1 [interleukin-2 (IL2), interferon gamma (IFN gamma)] and of TH2-type cytokines (IL4, IL6). Positive cells were usually observed in the subepithelial connective tissue, where most CD4+ cells were also detected. The density of IL2+ cells was significantly lower in high-grade SILs than in normal tissues taken either from the ectocervix or from the transformation zone. In contrast, significantly higher densities of IL4+ cells and, to a lesser degree, IL6+ cells were found in SIL biopsies compared with histologically normal tissues taken from the adjacent ectocervical region. A significantly higher IL4+/CD4+ cell ratio was also found in high-grade SILs (82 per cent) than in normal cervical biopsies taken from the transformation zone of healthy women showing squamous metaplasia (27 per cent). The elevated density of TH2+ cells in SIL biopsies was associated with both the expression of HLA-DR by keratinocytes and a diminished number of intraepithelial Langerhans' cells (CD1a+). In conclusion, the increased TH2+/CD4+ cell ratio in SIL biopsies suggest the presence, during cervical carcinogenesis, of a TH2 immunodeviation that could participate in the immunoescape of preneoplastic cervical keratinocytes.

L21 ANSWER 11 OF 16 MEDLINE

AN 1998225014 MEDLINE

TI Organotypic culture of HPV-transformed keratinocytes: a model for testing lymphocyte infiltration of (pre)neoplastic lesions of the uterine cervix.

AU Jacobs N; Moutschen M P; Franzen-Detrooz E; Boniver V; Boniver J; Delvenne P

SO VIRCHOWS ARCHIV, (1998 Apr) 432 (4) 323-30.
Journal code: BZD. ISSN: 0945-6317.

AB The aim of our study was to establish the relevance of an in vitro model for analysing the ability of human lymphocytes to infiltrate human papillomavirus (HPV)-associated (pre)neoplastic lesions of the uterine cervix. To mimic these lesions, we have used the organotypic raft culture of HPV-transformed keratinocytes (SiHa). The SiHa organotypic raft culture was co-cultured with resting or prestimulated (IL-2 or IL-2+anti-CD3 mAb) allogeneic peripheral blood mononuclear cells (PBMC) for 24 and 72 h. The majority of

infiltrating cells were T lymphocytes. Occasional NK cells were also identified. The stimulation with IL-2+anti-CD3 mAb induced the highest number of infiltrating cells, with the maximum lymphocyte infiltration observed after 24 h of co-culture. The lymphocyte infiltration was associated with an increased number of apoptotic cells in the organotypic cultures. The ability of PBMC and purified T cell and NK cell populations to lyse HPV-transformed keratinocytes was also investigated on monolayer cultures. As expected in an allogenic model, the highest cytotoxicity was mediated by NK cells activated by IL-2 or IL-2+anti-CD3 mAb. The cytotoxic activity of T cells was weak but, interestingly, increased in the presence of phytohaemagglutinin A (PHA), assuming that T cells were able to kill HPV-infected keratinocytes when a bridge between T cells and keratinocytes was provided. In conclusion, the organotypic culture of HPV-transformed keratinocytes may provide an effective in vitro model for investigating novel T cell-based immunotherapy protocols for the treatment of HPV-associated lesions.

L21 ANSWER 12 OF 16 MEDLINE
AN 97285700 MEDLINE
TI Cell mediated immunity induced in mice by HPV 16 L1 virus-like particles.
AU Dupuy C; Buzoni-Gatel D; Touze A; Le Cann P; Bout D; Coursaget P
SO MICROBIAL PATHOGENESIS, (1997 Apr) 22 (4) 219-25.
Journal code: MIC. ISSN: 0882-4010.
AB Recombinant human papillomavirus (HPV) type 16 L1 virus-like particles (VLPs) expressed in the baculovirus system were used to investigate the cellular immune response to human papillomavirus type 16. The cell-mediated immune response was evaluated through immunization of mice with HPV 16 L1 virus-like particles using a lymphoproliferation assay and cytokine production and cytometric analysis of lymphocyte subsets. A significant proliferative response was observed which was associated with secretion of both interferon-gamma and interleukin-2. FACS analysis of splenic lymphocytes revealed that CD8+ T-cells were increased in the immunized mice. These results demonstrate that HPV 16 L1 VLPs induce a T-cell response characterized by a Th1 profile and confirm that the HPV 16 VLP is a reasonable candidate for vaccine development.

L21 ANSWER 13 OF 16 MEDLINE
AN 97169198 MEDLINE
TI Cytokine production patterns in cervical intraepithelial neoplasia: association with human papillomavirus infection [see comments].
AU Clerici M; Merola M; Ferrario E; Trabattoni D; Villa M L; Stefanon B; Venzon D J; Shearer G M; De Palo G; Clerici E
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1997 Feb 5) 89 (3) 245-50.
Journal code: J9J. ISSN: 0027-8874.
AB BACKGROUND: Genital infection with certain strains of human

papillomavirus (HPV) is associated with a high risk of malignant transformation, and HPV-associated cervical intraepithelial neoplasia (CIN) can become invasive cancer. Host factors are critical in regulating tumor growth, and cytokines that modulate immunologic control may be of particular importance. The type 1 cytokines interleukin 2 (IL-2) and interferon gamma (IFN gamma) are immunostimulatory and are thus capable of limiting tumor growth. The type 2 cytokines interleukin 4 (IL-4) and interleukin 10 (IL-10) are immunoinhibitory and are thus capable of stimulating tumor growth. PURPOSE: We analyzed the production of cytokines by peripheral blood mononuclear cells (PBMCs) in women with CIN associated with localized or extensively spread HPV infection. METHODS: Thirty women diagnosed with CIN and 10 age- and sex-matched healthy control subjects were enrolled in the study conducted at Istituto Nazionale Tumori, Milan, Italy. The following parameters were analyzed: 1) HPV infection of the cervix and other sites of the lower genital tract by colposcopic, cytologic, and histologic examinations; 2) HPV typing; 3) in vitro production of IL-2 by PBMCs in response to stimulation with soluble antigen (influenza [FLU] antigen) or to cell-associated human leukocyte antigen (HLA) alloantigen; and 4) in vitro production of the type 1 cytokines IL-2 and IFN gamma and of the type 2 cytokines IL-4 and IL-10 by PBMCs in response to mitogen stimulation. Statistical significance was determined by nonparametric tests (two-sided). RESULTS: High-grade CIN associated with HPV infection was detected in all case patients, and HPV type 16 or 18 infection was detected in cervical tissue of 21 (70%) of 30 case patients. HPV infection that had spread to other sites of the lower genital tract, thus resulting in more extensive disease, was detected in 16 (53%) of the 30 individuals with CIN, whereas HPV infection was limited to the portio in 14 (47%). IL-2 production by PBMCs in response to stimulation with soluble antigen or HLA alloantigen was reduced in the group with extensive disease compared with that in the group with localized disease or with that in healthy control subjects. In contrast, IL-4 and IL-10 production in response to mitogen stimulation was elevated in the group with extensive disease compared with that in the group with localized disease or with that in healthy control subjects. The highest production of IL-4 and IL-10 was detected in patients with HPV infection that had extended beyond the genital tract. CONCLUSIONS: CIN is characterized by different immunologic profiles, in which HPV infection is or is not confined to the portio. Production of cytokines that mainly enhance potentially protective cell-mediated immunity is defective in the women in whom extended HPV infection was observed. A pronounced shift from type 1 to type 2 cytokine production is associated with more extensive HPV infection. IMPLICATIONS: These data reinforce the need for detailed analyses of immune dysregulation in CIN patients. They also suggest the potential usefulness of the cytokine assays for determining prognosis or deciding whether cytokine-based therapy is indicated.

L21 ANSWER 14 OF 16 MEDLINE
AN 96354617 MEDLINE
TI Interleukin 2 production in vitro by peripheral lymphocytes in response to human papillomavirus-derived peptides: correlation with cervical pathology.
AU Tsukui T; Hildesheim A; Schiffman M H; Lucci J 3rd; Contois D; Lawler P; Rush B B; Lorincz A T; Corrigan A; Burk R D; Qu W; Marshall M A; Mann D; Carrington M; Clerici M; Shearer G M; Carbone D P; Scott D R; Houghten R A; Berzofsky J A
SO CANCER RESEARCH, (1996 Sep 1) 56 (17) 3967-74.
Journal code: CNF. ISSN: 0008-5472.
AB Human papillomavirus (HPV) is believed to be the major cause of cervical cancer. To investigate whether a cellular immune response, especially a T helper type 1 response, is related to the natural defense against HPV-related cervical lesions, the interleukin 2 response of peripheral blood lymphocytes in vitro to overlapping peptides from HPV-16 E6 and E7 oncoproteins was compared with the degree of cervical cytological abnormality among 140 women in a cross-sectional study. We compared 66 women diagnosed with low-grade squamous intraepithelial lesions (LSIL), 21 with high-grade squamous intraepithelial lesions (HSIL), and 28 with invasive cervical cancer with 25 women who were cytologically normal but previously HPV-16 DNA positive. The fraction showing strong interleukin 2 production against HPV-16 peptides was greatest among cytologically normal women (35%) and declined with increasing disease severity [LSIL] (20%), HSIL, (17%), and cancer patients (7%); X2 test P for the trend = 0.02], whereas the responses against a recall influenza antigen were not significantly different among groups. Our finding suggests that a T helper lymphocyte type 1 response to HPV antigens is associated with disease status. This result may reflect a targeted effect of the disease on immune function or a protective effect of the immune response against disease progression.

L21 ANSWER 15 OF 16 MEDLINE
AN 96307463 MEDLINE
TI [Association of interleukin 2 and interferon alpha in the management of cervical condylomatosis].
Associazione di interleuchina-2 ed interferone-alpha nel trattamento della condilomatosi della cervice uterina.
AU Zarcone R; Bellini P; Cardone G; Barletta E; Vicinanza G
SO MINERVA GINECOLOGICA, (1996 Mar) 48 (3) 111-3.
Journal code: N66. ISSN: 0026-4784.
AB At present the therapy of cervical condylomatosis is based on the use of interferon because the HPV types responsable for condyloma inhibit the immunitary system. But many A. studying the effects of IFN have found that at high concentration it has an immunosuppressive action. The aim of the present study was to evaluate if interleukin-2 associated with IFN is useful in avoiding

this negative effect by improving the efficacy of cervical condylomatosis therapy. We treated 25 women suffering from cervical condyloma with increasing doses of IL-2 injected intralesionally and associated with natural alpha-IFN injected intramuscularly. The duration of the whole therapy was six weeks. We evaluated the percentage of inflammatory cells in peripheral blood before and after treatment. The per-cent number of lymphocytes, eosinophils and lymphoblasts was increased by 27%, 88% and 40%, respectively. The clinical response to the therapy was total in 14 cases, partial in 9 cases and unsuccessful in 2 cases. These data suggested that combination therapy with interleukin-2 and alpha-IFN for the treatment of patients with cervix condylomatous is successful.

L21 ANSWER 16 OF 16 MEDLINE
AN 95376807 MEDLINE
TI A vaccine conjugate of 'ISCAR' immunocarrier and peptide epitopes of the E7 cervical cancer-associated protein of human papillomavirus type 16 elicits specific Th1- and Th2-type responses in immunized mice in the absence of oil-based adjuvants.
AU Tindle R W; Croft S; Herd K; Malcolm K; Geczy A F; Stewart T; Fernando G J
SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 Aug) 101 (2) 265-71. Journal code: DD7. ISSN: 0009-9104.
AB TraT protein, known as ISCAR (= Immunostimulatory Carrier), is one of a family of integral membrane proteins (Imps) of Escherichia coli representing powerful carrier molecules which when injected into experimental animals generate substantial antibody and T proliferative responses to molecules conjugated to it. We extend these findings to show that ISCAR functions to stimulate Th1- and Th2-type responses, including specific cytotoxic T cells and tumour protection. We report here that by conjugating to ISCAR a 19mer peptide containing linear B epitopes, a T helper (Th) epitope, and a H-2b-restricted T cytotoxic (CTL) epitope of E7 protein of human papillomavirus type 16 (HPV16), and immunizing C57B1/6 (H-2b) mice, we elicited (i) specific IgG2a and IgG1 antibodies; (ii) IL-2 and IL-4 production by specifically recalled lymph node cells in vitro; (iii) cytotoxic T lymphocytes which specifically killed both E7 peptide-pulsed, and whole E7 gene-transfected tumour target cells; and (iv) in vivo protection against an E7 gene-transfected tumour cell inoculum. These findings have implications for the design of vaccines to stimulate immune responses to endogenously processed target antigens (e.g. tumour-associated antigens) without the unwanted side effects of oil-based adjuvants. In addition they support the case for a E7-targeted therapeutic vaccine for HPV-associated human cervical cancer.

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CESSION NUMBER: 96073214 EMBASE
DOCUMENT NUMBER: 1996073214
TITLE: **IL-2** as adjuvant for vaccination with cells malignantly converted by HPV 16 or 3-MC.
AUTHOR: Bubenik J.; Simova J.; Vondrys P.; Vonka R.; Kitasato H.; Bostik P.; Vonka V.
CORPORATE SOURCE: Institute of Molecular Genetics, Academy of Sciences Czech Republic, Flemingovo nam. 2,166 37 Prague 6, Czech Republic
SOURCE: International Journal of Oncology, (1996) 8/3 (477-481). ISSN: 1019-6439 CODEN: IJONES
COUNTRY: Greece
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Experiments were designed to investigate the effects of murine recombinant **IL-2** used as adjuvant for tumour vaccines in two model systems. The first system I employed the Syrian hamster K3/II cell line transformed malignantly in vitro with DNA from **E6-E7** oncogenes from HPV 16 and transplanted in Syrian hamsters. The second system made use of murine sarcoma Mc12 induced with MC and transplanted in histocompatible mice. Both rumours were previously shown to express TRA capable of inducing transplantation resistance. It has been demonstrated here that the effect of the immunization in both tumour model systems could be substantially increased by **IL-2** injected repeatedly at the site of vaccination. Some of the experimental mice were sacrificed after immunization and their spleen as well as regional lymph node cells were used for phenotypic analysis. **IL-2** administration was found to be accompanied with an increase of TCR.alpha..beta.+, CD4+ T cells in the spleen. Also in regional lymph nodes the T cell subsets showed a characteristic kinetics due to **IL-2** administration. Following the **IL-2 treatment**, the percentage of lymph node TCR.alpha..beta.+, CD4+ and CD8+ cells dropped to less than half of the pretreatment values and then again gradually increased. No such kinetics was observed in vaccinated mice that did not receive **IL-2**. These results suggest that local administration of **IL-2** at the site of vaccination elicits, in addition to the reaction in regional lymph nodes, a systemic reaction detectable in the spleen; they also suggest that the increase of CD4+, TCR.alpha..beta.+ T splenocytes may play an important role in the mechanism of the observed adjuvant effect of **IL-2**. The adjuvant **IL-2** effect augmentin the function of cell vaccines expressing HPV 16E-**E7** oncoprotein deserves further studies, particularly with regard to its prospective utilization for **treatment** of human cervical carcinoma.

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L14 ANSWER 1 OF 18 MEDLINE
AN 95038298 MEDLINE
DN 95038298
TI Recombinant MUC 1 vaccinia virus: a potential vector for immunotherapy of breast cancer.
AU **Balloul J M**; Acres R B; Geist M; Dott K; Stefani L; Schmitt D; Drillien R; Spehner D; McKenzie I; Xing P X; et al
CS INSERM U74, Universite Louis Pasteur, Strasbourg, France.
SO CELLULAR AND MOLECULAR BIOLOGY, (1994) 40 Suppl 1 49-59.
Journal code: BNA.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
AB Breast cancer is considered as the major cause of mortality by cancer for women. Even if chemotherapy, radiotherapy and surgery have improved the life expectancy of patients bearing tumours, breast cancer is responsible for the death of 42,000 women per year in USA and 25,000 women in France. In this context, cancer vaccines may add an attractive alternative therapeutic strategy to the current existing treatments. We describe here the construction of recombinant vaccinia viruses co-expressing a tumour associated antigen (MUC 1) and an "adjuvant" cytokine, which have potential applications in the active immunotherapy of breast cancer. Indeed, recombinant vaccinia viruses have been extensively used during the past decade to induce a protective response against a whole variety of pathogens, and has proven to be of great value in the elicitation of a cellular immune response leading to the rejection of tumour grafts in mouse models.
CT Check Tags: Animal; Female; Human
*Antigens, Neoplasm: GE, genetics
Base Sequence
Breast Neoplasms: IM, immunology
*Breast Neoplasms: TH, therapy
Combined Modality Therapy
Cytokines: GE, genetics
DNA, Complementary: GE, genetics
Genetic Vectors
*Immunotherapy: MT, methods
*Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: IM, immunology
Mice
Molecular Sequence Data
*Mucins: GE, genetics
*Mucins: IM, immunology
Recombinant Proteins: GE, genetics
Recombinant Proteins: IM, immunology
Repetitive Sequences, Nucleic Acid
*Vaccinia Virus: GE, genetics
*Vaccinia Virus: IM, immunology
CN 0 (Antigens, Neoplasm); 0 (Cytokines); 0 (CA-15-3 Antigen); 0 (DNA, Complementary); 0 (Genetic Vectors); 0 (Membrane Glycoproteins); 0 (Mucins); 0 (Recombinant Proteins)
GEN MUC 1

L14 ANSWER 2 OF 18 MEDLINE

AN 94107852 MEDLINE
DN 94107852
TI Vaccinia virus MUC1 immunization of mice: immune response and protection against the growth of murine tumors bearing the MUC1 antigen.
AU Acres R B; Hareuveni M; **Balloul J M**; Kieny M P
CS Department of Immunology, Transgene S.A., Strasbourg, France..
SO JOURNAL OF IMMUNOTHERAPY, (1993 Aug) 14 (2) 136-43.
Journal code: AZ0. ISSN: 1053-8550.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
AB MUC1 is a mucin found on the apical surfaces of some normal mammalian mucin-secreting cells. It is characterized by heavy glycosylation and a 20-amino-acid tandem repeat segment. In most cases of human breast adenocarcinoma, this antigen is overexpressed. Moreover, abnormal glycosylation exposes a novel peptide epitope within the tandem repeat, such that antibodies to this epitope can distinguish normal from malignant adenocarcinomatous breast tissue. We have constructed a vaccinia virus (VV) that carries the cDNA for the MUC1 antigen. Murine and human cells infected with this virus express the MUC1 molecule, with three to four tandem repeats per molecule and with the tumor-associated epitopes exposed. Mice immunized with this virus produce antibodies that recognize MUC1 outside the tandem repeat, within the tandem repeat, and within the tumor-associated protein core epitope. Tumorigenic P815 (DBA) and 3T3 (BALB/c) cells have been transfected with MUC1. Thirty percent of DBA mice immunized with VV-MUC1 are protected from growth of P815-MUC1 tumors when implanted with 10(5) cells. Immunized BALB/c mice show a late development of transfected 3T3 tumor cells. Immunized mice show a moderate MUC1-specific IgG titer, but it cannot be correlated with subsequent tumor rejection. No evidence for a MUC1-specific cytotoxic T lymphocyte response has been found after immunization with VV-MUC1.
CT Check Tags: Animal
Antibody Formation
*Antigens, Neoplasm
*Antigens, Viral: IM, immunology
Cell Division: IM, immunology
Disease Models, Animal
*Immunization
Mice
Mice, Inbred BALB C
Mice, Inbred DBA
*Mucins: IM, immunology
Neoplasm Transplantation
*Neoplasms, Experimental: IM, immunology
*Vaccinia Virus: IM, immunology
CN 0 (Antigens, Neoplasm); 0 (Antigens, Viral); 0 (Mucins)